In one aspect, the present invention is directed to novel polypeptides and polynucleotides produced by recombination of nucleic acids encoding seven different mammalian B7-1 polypeptides -- human, rhesus monkey, baboon, orangutan, cow, cat and rabbit B7-1. See, e.g., specification, page 178, lines 9-18; Examples I-VIII, page 178, line 8 to page 236, line 8. In one aspect, the present invention provides novel polypeptides and polynucleotides encoding polypeptides that: 1) bind CD28 with at least equal or greater affinity than human B7-1 binds CD28 receptor, 2) that bind CTLA-4 receptor with less affinity than human B7-1 binds CTLA-4 receptor, and/or 3) induce T cell proliferation or T cell activation. See, e.g., specification at page 108, lines 14-22; page 109, line 25 to page 110, line 6.

The amino acid and nucleic acid sequences for human B7-1, which are shown in SEQ ID NOS:278 and 273, respectively, are well known. See, e.g., specification at page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 285; Figures 2A-2H. The polypeptide sequence of human B7-1 comprises 288 amino acids. *Id.* The predicted signal peptide, extracellular domain (ECD), transmembrane domain, cytoplasmic domain, and mature domain subsequences of human B7-1 are also known. *Id.* According to one study of the full-length human B7-1 polypeptide, the predicted signal peptide comprises amino acid residues 1-34, the predicted ECD comprises amino acid residues 35-242, the predicted transmembrane domain comprises amino acid residues 243-263, and the predicted cytoplasmic domain comprises amino acid residues 264-288 of human B7-1. *Id.* The predicted mature form of human B7-1 comprises about 254 amino acids corresponding to amino acid residues 35-288 of the human B7-1 polypeptide (i.e., the predicted mature domain comprises full-length B7-1 polypeptide sequence without the signal peptide). *Id.* The nucleic acid encoding human B7-1, as shown in SEQ ID NO:273 (page 285), includes 864 nucleic acid residues which encode the 288-amino acid sequence of human B7-1, plus 3 nucleic acid residues at the C-terminus corresponding to a stop codon (e.g., TGA). See, e.g., SEQ ID NO:273.

For each novel polypeptide of the invention (e.g., a CD28BP polypeptide), the amino acid residues of the polypeptide sequence that correspond to the predicted signal peptide, extracellular domain, transmembrane domain, cytoplasmic domain, and mature domain are readily determined in one aspect by comparison with the corresponding known subsequences of human B7-1 polypeptide (SEQ ID NO:278). See, e.g., specification, page 22, lines 6-15, page 121, line 12 to page 123, line 27; Figures 2A-2H. For each nucleic acid of the invention that encodes a polypeptide of the invention (e.g., a CD28BP polypeptide), the nucleotide residues encoding the predicted signal

peptide, ECD, transmembrane domain, cytoplasmic domain, and mature form are similarly determined in one aspect by comparison with the human B7-1 nucleotide sequence. See, e.g., specification, page 27, lines 13-16; page 122, lines 7-27.

Support for new claims 259-381 is found throughout the specification. Support for new claims 259-381 in the specification is indicated below, but is not limited to the pages indicated below; such pages and lines are simply exemplary of the support provided in the specification. Additional passages in the specification also support the claims.

Support for claims 259 and 260 is provided throughout the specification, including at, but not limited to, e.g., original claims 1-2; page 9, line 19 to page 10, line 18; page 43, lines 10-15; page 87, lines 12-31; page 21, line 27 to page 22, line 5; page 62, lines 15-23.

Support for new claim 261 is at, e.g., original claim 2; page 9, line 19 to page 10, line 18; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H. For example, as shown in Fig. 2A-2H, based upon a comparison with the human B7-1 polypeptide sequence (SEQ ID NO:278), in one aspect the CD28BP-15 polypeptide sequence (SEQ ID NO:66) comprises the following predicted subsequences: the predicted signal peptide comprises amino acid residues 1-34, the predicted extracellular domain (ECD) comprises at least amino acid residues 35-244, the predicted transmembrane domain comprises at least amino acid residues 245-268, and the predicted cytoplasmic domain comprises at least amino acid residues 268-303.

Support for new claim 262 is at, e.g., Figure 8B (*see originally filed informal drawing for Figure 8B and corrected formal drawing for Figure 8B submitted herewith*); Table 5 and page 209, lines 6-13; page 198, line 30 to page 199, line 11; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H. As indicated therein, in one aspect the predicted transmembrane domain of CD28BP-15 (SEQ ID NO:66) comprises at least amino acid residues 246-272 (*see dashed line indicating transmembrane domain in originally filed informal drawing for Figure 8B and corrected formal drawing for Figure 8B submitted herewith*) and the predicted extracellular domain of SEQ ID NO:66 comprises at least amino acid residues 35-245. Table 5 and page 209, lines 6-13 also indicate that in one aspect for CD28BP-15 (SEQ ID NO:66), the predicted signal peptide comprises residues 1-34, the predicted extracellular domain ends at amino acid residue 245 and thus comprises residues 35-245. The predicted transmembrane domain in this embodiment thus begins at amino acid

residue 246.

Support for new claim 263, is at, e.g., original claim 3; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H.

Support for new claim 264 is at, e.g., original claim 29; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; page 209, lines 6-13.

Support for new claims 265-266 is at, e.g., original claim 30; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; page 209, lines 6-13.

Support for new claims 267-270 is at, e.g., original claim 31; Figure 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H. As shown, e.g., by comparison with human B7-1 polypeptide (see Figs. 2A-2H), the predicted transmembrane domain of SEQ ID NO:66 comprises in one aspect at least amino acid residues 245-268 of SEQ ID NO:66. As shown in Figure 8B, e.g., the predicted transmembrane domain of SEQ ID NO:66 comprises in another aspect at least amino acid residues 246-272 (see dashed line in Figure 8B).

Support for new claims 271-274 is at, e.g., original claim 31; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H. As shown, e.g., by comparison with human B7-1 polypeptide (see Figs. 2A-2H), the predicted cytoplasmic domain of SEQ ID NO:66 comprises in one aspect at least amino acid residues 269-303 of SEQ ID NO:66. As shown in Figure 8B, e.g., the predicted cytoplasmic domain of SEQ ID NO:66, which follows the transmembrane domain, comprises in another aspect at least amino acid residues 273-303.

Support for new claims 275-276 is at, e.g., page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Fig. 8B; page 198, line 30 to page 199, line 11; Figs. 2A-2H. As shown, e.g., by comparison with human B7-1 polypeptide (see Figs. 2A-2H), the predicted mature domain of SEQ ID NO:66 comprises in one aspect at least amino acid residues 35-303 of SEQ ID NO:66. See also Figure 8B.

Support for new claim 277 is at, e.g., page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198,

line 30 to page 199, line 11. As shown, e.g., by comparison with human B7-1 polypeptide (see Figs. 2A-2H), the predicted signal peptide, extracellular domain and transmembrane domain of SEQ ID NO:66 comprises in one aspect at least amino acid residues 1-68 of SEQ ID NO:66. As shown in Fig. 8B, e.g., the predicted signal peptide, extracellular domain and transmembrane domain of SEQ ID NO:66 comprises in another aspect at least amino acid residues 1-272.

Support for new claims 278-279 is at, e.g., original claim 4; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H.

Support for new claim 280 is at, e.g., original claim 5. Support for new claim 281 is at, e.g., original claim 6; and page 108, lines 16-20. Support for new claim 282 is at, e.g., original claim 7; page 108, lines 16-20. Support for new claim 283 is at, e.g., original claim 10.

Support for new claim 284 is at, e.g., page 9, lines 19-23; page 22, lines 6-14; ; page 21, lines 27-31; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 62, lines 15-19; page 198, line 30 to page 199, line 11page 121, line 12 to page 123, line 18; page 204, lines 1-7; Figs. 2A-2H and Fig. 8B.

Support for new claim 285 is at, e.g., Fig. 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H.

Support for new claims 286-287 is at, e.g., original claims 12, 29, 31; page 87, lines 12-31; page 9, lines 19-23; page 121, line 12 to page 123, line 18.

Support for new claim 288 is at, e.g., page 21, lines 27-30. Support for new claim 289 is at, e.g., original claim 38. Support for new claim 290 is at, e.g., original claim 39.

Support for new claim 291 is at, e.g., original claims 19, 21, and 22; page 111, line 1 to page 112, line 2. Support for new claim 292 is at, e.g., original claim 21. Support for new claim 293 is at, e.g., original claim 23. Support for new claims 294-295 is at, e.g., original claims 24-25, respectively. Support for new claim 296 is at, e.g., original claim 26; page 22, lines 6-14; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H.

Support for new claim 297 is at, e.g., original claim 4; page 87, lines 12-31; page 121, line 12 to page 123, line 18; page 21, lines 27-31; page 62, lines 15-19.

Support for new claim 298 is at, e.g., original claim 41. Support for new claim 299 is at, e.g., original claim 31; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-

31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23.

Support for new claim 300 is at, e.g., original claim 31; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23. Support for new claim 301 is at, e.g., Table 5 and page 209, lines 6-13; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, lines 19-23.

Support for new claims 302-303 is at, e.g., original claims 43, 46, 47, 50; page 9, line 19 to page 10, line 18; page 87, lines 3-11; page 21, lines 27-31; page 62, lines 15-19; page 121, line 12 to page 123, line 18.

Support for new claims 304-305 is at, e.g., original claim 46; page 9, line 19 to page 10, line 18; page 22, lines 6-14; page 26, line 27 to page 27, line 16; page 87, lines 12-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Figure 8B; page 9, line 19 to page 10, line 18

Support for new claim 306 is at, e.g., original claim 46; page 9, line 19 to page 10, line 18; page 22, lines 6-14; page 87, lines 1-31; page 121, line 12 to page 123, line 18.

Support for new claims 307-308 is at, e.g., original claim 46; page 22, lines 6-14; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 9, line 19 to page 10, line 18; page 209, lines 6-13.

Support for new claims 309-316 is at, e.g., original claim 46; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claim 317 is at, e.g., original claim 43; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; page 9, line 19 to page 10, line 18; Fig. 8B; page 198, line 30 to page 199, line 11; Figs. 2A-2H.

Support for new claims 318-320 is at, e.g., original claims 43, 46; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claim 321 is at, e.g., original claim 43; page 28, lines 5-7; page 87, 1-31; page 53, lines 16-24; page 9, line 19 to page 10, line 18. Support for new claim 322 is at, e.g.,

original claims 43, 46, 47, and 50; page 87, lines 1-31. Support for new claim 323 is at, e.g., original claim 48. Support for new claim 324 is at, e.g., original claim 49.

Support for new claims 325-326 is at, e.g., original claims 46, 47, and 50; page 209, Table 5 and lines 6-13; page 87, lines 1-31; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claim 327 is at, e.g., original claim 46; page 22, lines 6-14; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs 2A-2H. Support for new claim 328 is at, e.g., original claim 43; page 28, lines 5-7; page 87, 1-31; page 53, lines 16-23; page 9, line 19 to page 10, line 18; Figs. 2A-2H; page 121, line 12 to page 123, line 18; page 209, lines 6-13.

Support for new claims 329-331 is at, e.g., original claim 46, page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; page 53, lines 16-23; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claims 332-334 is at, e.g., original claim 46; page 22, lines 6-14; page 26, line 26 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18; page 53, lines 16-23. Support for new claims 335-336 is at original claims 43 and 50; page 121, line 12 to page 123, line 18.

Support for new claim 337 is at, e.g., original claim 46; page 87, lines 1-31; page 209, Table 5 and lines 6-13; Figs. 2A-2H; page 121, line 12 to page 123, line 18; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18; page 22, lines 6-14; page 26, line 27 to page 27, line 10.

Support for new claim 338 is at, e.g., original claim 46; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claim 340 is at, e.g., original claim 43; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18.

Support for new claims 341-344 is at, e.g., original claims 70-71; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs.

2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18; page 209, Table 5 and lines 6-13.

Support for new claims 345-347 is at, e.g., original claims 58 and 59; page 16, lines 18-20; page 22, lines 6-14; page 26, line 27 to page 27, line 10; page 87, lines 1-31; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18; page 209, Table 5 and lines 6-13; page 161, lines 20-31.

Support for new claims 348-352 and 358-362 is at, e.g., original claims 60-64, respectively; page 209, Table 5 and lines 6-13; page 87, lines 1-31; page 26, line 27 to page 27, line 10; page 121, line 12 to page 123, line 18; Figs. 2A-2H; Fig. 8B; page 198, line 30 to page 199, line 11; page 9, line 19 to page 10, line 18. Support for new claim 359 is also at, e.g., page 67, line 12 to page 69, line 3.

Support for new claims 353 and 363 is at, e.g., original claim 66; page 162, lines 20-24; page 49, lines 16-19; Fig. 28B; page 209, Table 5 and lines 6-13; page 87, lines 1-31.
Support for new claims 354-355 and 364-365 is at, e.g., original claims 64-65, respectively. Support for new claims 356 and 366 is at, e.g., original claim 68. Support for new claims 357 and 367 is at, e.g., original claim 69; page 57, lines 12-23.

Support for new claims 368-369 is at, e.g., original claims 171-173, respectively; page 127, line 20 to page 132, line 29.

Support for new claim 370 is at, e.g., original claim 174. Support for new claim 371 is at, e.g., original claim 176. Support for new claim 372 is at, e.g., original claim 176.

Support for new claim 373 is at, e.g., page 17, lines 11-17; page 18, lines 14-19; page 19, lines 6-13; page 145, lines 22-30.

Support for new claims 374-375 and 378 is at, e.g., page 146, line 26 to page 147; line 3; page 166, lines 1-8; page 167, lines 14-16. Support for new claims 376-377 is at, e.g., page 34, lines 6-11; page 145, lines 22-30; page 146, line 26 to page 147; line 3.

Support for new claim 379 is at, e.g., original claims 223 and 257; page 18, lines 14-19; page 146, line 26 to page 147; line 3.

Support for new claim 380 is at, e.g., original claim 223; page 166, lines 1-8; page 167, lines 14-16; page 140, line 25 to page 153, line 10.

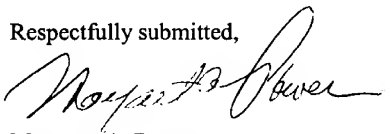
Support for new claim 381 is at, e.g., Table 5 and page 209, lines 6-13.

C nclusi n

In view of the foregoing, Applicants believe that all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 298-5809.

Respectfully submitted,



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APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING AMENDMENT MADE TO THE CLAIMS OF USSN 09/888,324 WITH ENTRY OF THIS AMENDMENT

All of original claims 1-258 have been cancelled without prejudice to subsequent renewal. New claims 259-381 have been added as shown below. This set of new claims comprises a complete set and clean version of all currently pending claims.

--259. (New) An isolated or recombinant polypeptide comprising an extracellular domain, said extracellular domain comprising an amino acid sequence having at least about 91% sequence identity to a subsequence of the polypeptide sequence set forth in SEQ ID NO:66, wherein the subsequence is the extracellular domain of SEQ ID NO:66, and wherein the isolated or recombinant polypeptide has a human CD28/human CTLA-4 binding affinity ratio about equal to or greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 when expressed on a cell or bound to a cell membrane.

260. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide is expressed on a cell or bound to a cell membrane.

261. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an extracellular domain which comprises an amino acid sequence having at least about 95% sequence identity to the extracellular domain of SEQ ID NO:66, wherein said extracellular domain of SEQ ID NO:66 comprises at least amino acid residues 35-244 of SEQ ID NO:66.

262. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an extracellular domain which comprises an amino acid sequence having at least about 95% sequence identity to the extracellular domain of SEQ ID NO:66, wherein the extracellular domain of SEQ ID NO:66 comprises at least amino acid residues 35-245 of SEQ ID NO:66.

263. (New) The isolated or recombinant polypeptide of claim 261, wherein the polypeptide comprises an extracellular domain comprising at least amino acid residues 35-244 of SEQ ID NO:66.

264. (New) The isolated or recombinant polypeptide of claim 261, wherein the polypeptide comprises an extracellular domain comprising at least amino acid residues 35-244 of SEQ ID NO:66.

264. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide further comprises a signal peptide.

265. (New) The isolated or recombinant polypeptide of claim 264, wherein the signal peptide comprises an amino acid sequence that has at least about 90% sequence identity to the amino acid sequence comprising residues 1-34 of SEQ ID NO:66.

266. (New) The isolated or recombinant polypeptide of claim 264, wherein the signal peptide has an amino acid sequence comprising amino acid residues 1-34 of SEQ ID NO:66.

267. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises a transmembrane domain.

268. (New) The isolated or recombinant polypeptide of claim 267, wherein the polypeptide comprises the transmembrane domain of SEQ ID NO:66.

269. (New) The isolated or recombinant polypeptide of claim 268, wherein the transmembrane domain comprises an amino acid sequence having at least about 90% sequence identity to an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

270. (New) The isolated or recombinant polypeptide of claim 269, wherein the transmembrane domain comprises an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

271. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide further comprises a cytoplasmic domain.

272. (New) The isolated or recombinant polypeptide of claim 271, wherein the polypeptide comprises the cytoplasmic domain of SEQ ID NO:66.

273. (New) The isolated or recombinant polypeptide of claim 271, wherein the cytoplasmic domain comprises an amino acid sequence having at least about 90% sequence identity to an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

274. (New) The isolated or recombinant polypeptide of claim 273, wherein the cytoplasmic domain comprises an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

275. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an amino acid sequence having at least about 90% sequence identity to the amino acid sequence comprising a mature domain of SEQ ID NO:66.

276. (New) The isolated or recombinant polypeptide of claim 275, wherein the mature domain comprises amino acid residues 35-303 of SEQ ID NO:66.

277. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an amino acid sequence having at least about 90% sequence identity to the amino acid sequence corresponding to the signal peptide, extracellular domain and transmembrane domain of SEQ ID NO:66 which comprises at least amino acid residues 1-268 or 1-272 of SEQ ID NO:66.

278. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has at least about 91% sequence identity to the full length amino acid sequence of SEQ ID NO:66.

279. (New) The isolated or recombinant polypeptide of claim 278, wherein the polypeptide comprises the full length amino acid sequence of SEQ ID NO:66.

280. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1.

281. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a binding affinity for CD28 that is at least about equal to or greater than the binding affinity of human B7-1 for CD28.

282. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a binding affinity for CTLA-4 that is less than the binding affinity of human B7-1 for CTLA-4.

283. (New) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has an ability to induce a T-cell proliferation response about equal to or greater than the T-cell proliferation response induced by human B7-1.

284. (New) An isolated or recombinant polypeptide comprising an extracellular domain, said extracellular domain comprising an amino acid sequence having at least about 91% sequence identity to a subsequence of SEQ ID NO:66, said subsequence comprising at least amino acid residues 35-244 or 35-245 of SEQ ID NO:66, wherein said polypeptide induces a T-cell proliferation response about equal to or greater than the T-cell proliferation response induced by human B7-1 when expressed on a cell or bound to a cell membrane.

285. (New) The isolated or recombinant polypeptide of claim 284, wherein the subsequence comprises at least amino acid residues 35-245 of SEQ ID NO:66.

286. (New) The isolated or recombinant polypeptide of claim 284, wherein the polypeptide comprises one or more of a signal peptide, transmembrane domain, and cytoplasmic domain.

287. (New) The isolated or recombinant polypeptide of claim 286, wherein the polypeptide comprises an amino acid sequence having at least about 95% sequence identity to the full length amino acid sequence of SEQ ID NO:66.

288. (New) The isolated or recombinant polypeptide of claim 259, wherein the cell is an antigen-presenting cell.

289. (New) The polypeptide of claim 259, comprising at least one modified amino acid.

290. (New) The polypeptide of claim 288, wherein the modified amino acid is selected from: a glycosylated amino acid, a PEGylated amino acid, a farnesylated amino acid, an acetylated amino acid, a biotinylated amino acid, an amino acid conjugated to a lipid moiety, and an amino acid conjugated to an organic derivatizing agent.

291. (New) An isolated or recombinant polypeptide comprising an amino acid sequence according to the formula:

MGHTM-X6-W-X8-SLPPK-X14-PCL-X18-X19-X20-QLLVLT-X27-LFYFCSGITPKSVTKRVKETVMLSCDY-X55-TSTE-X60-LTSLRIYW-X69-KDSKMVLAILPGKVQVWPEYKNRTITDMNDN-X101-RIVI-X106-ALR-X110-SD-X113-GTYTCV-X120-QKP-X124-LKGAYKLEHL-X135-SVRLMIRADFPVP-X149-X150-X151-DLGNPSPNIRRLICS-X167-X168-X169-GFPRPHL-X177-WLENGEELNATNTT-X192-SQDP-X197-T-X199-LYMISSEL-X208-FNVTNN-X215-SI-X218-CLIKYGEL-X227-VSQIFPWSKPKQEPPIDQLPF-X249-VIIPVSGALVL-X261-A-X263-VLY-X267-X268-ACRH-

X273-ARWKRTRRNEETVGTE RLSPIYLGSAQSSG, or an extracellular domain subsequence thereof comprising amino acid residues at positions 35-244,

wherein the amino acid residue at position X6 is Lys or Glu; position X8 is Arg or Gly; position X14 is Arg or Cys; position X18 is Trp or Arg; position X19 is Pro or Leu; position X20 is Ser or Pro; position X27 is Asp or Gly; position X55 is Asn or Ser; position X60 is Glu or Lys; position X69 is Gln or Arg; position X101 is Pro or Leu; position X106 is Leu or Gln; position X110 is Pro or Leu; position X113 is Lys or Ser; position X120 is Val or Ile; position X124 is Val or Asp; position X135 is Thr or Ala; position X149 is Thr, Ser, or deleted; position X150 is Ile or deleted; position X151 is Asn or Thr; position X167 is Thr or deleted; position X169 is Ser or deleted; position X169 is Gly or deleted; position X177 is Cys or Tyr; position X192 is Val or Leu; position X197 is Gly or Glu; position X199 is Glu or Lys; position X208 is Gly or Asp; position X215 is His or Arg; position X218 is Ala or Val; position X227 is Ser or Leu; position X249 is Trp, Leu, or Arg; position X261 is Ala or Thr; position X263 is Val, Ala, or Ile; position X267 is Arg or Cys; position X268 is Pro or Leu; and position X273 is Gly or Val, and

wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio about equal to or greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 and/or induces a T-cell proliferation or activation response when expressed on a cell or bound to a cell membrane.

292. (New) The isolated or recombinant polypeptide of claim 291, wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio about greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1.

293. (New) The isolated or recombinant polypeptide of claim 291, wherein the polypeptide induces a T-cell proliferation response about equal to or greater than that induced by human B7-1.

294. (New) The isolated or recombinant polypeptide of claim 291, comprising three or more of: Lys at position X6; Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Asp at position X27; Asn at position X55; Leu at position X106; Pro at position X110; Lys at position X113; Val at position X120; Val at position X124; Thr at position X135; Asn at position X151; Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp

at position X249; Ala at position X261; Val at position X263; Arg at position X267; Pro at position X268; and Gly at position X273.

295. (New) The isolated or recombinant polypeptide of claim 294, comprising three or more of: Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Pro at position X110; Val at position X120; Val at position X124; Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp at position X249; Ala at position X261; and Val at position X263.

296. (New) The isolated or recombinant polypeptide of claim 295, comprising amino acid residues 35-244 of SEQ ID NO:66.

297. (New) An isolated or recombinant polypeptide comprising an amino acid sequence having at least about 91% sequence identity to the complete amino acid sequence set forth in SEQ ID NO:66, wherein said polypeptide when expressed on a cell or bound to a cell membrane has a human CD28/human CTLA-4 binding affinity ratio at least about equal to the human CD28/human CTLA-4 binding affinity ratio of human B7-1 or induces a T-cell proliferation or activation response.

298. (New) A composition comprising a polypeptide of claim 259 and a pharmaceutically acceptable excipient.

299. (New) An isolated or recombinant polypeptide comprising an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

300. (New) An isolated or recombinant polypeptide comprising an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

301. (New) The isolated or recombinant polypeptide of claim 264, wherein the polypeptide comprises an amino acid sequence comprising at least amino acid residues 1-244 or 1-245 of SEQ ID NO:66.

302. (New) An isolated or recombinant nucleic acid comprising a polynucleotide sequence that encodes a polypeptide comprising an extracellular domain, said extracellular domain comprising an amino acid sequence having at least about 91% sequence identity to a subsequence of the polypeptide sequence set forth in SEQ ID NO:66, wherein the subsequence is the extracellular domain of SEQ ID NO:66, and wherein the encoded polypeptide has a human CD28/human CTLA-4 binding affinity ratio about equal to or greater than the human CD28/human CTLA-4 binding

affinity ratio of human B7-1 or induces a T-cell proliferation or activation response when expressed on a cell or bound to a cell membrane, or a complementary polynucleotide sequence thereof.

303. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide is expressed on a cell or bound to a cell membrane.

304. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises an extracellular domain comprising an amino acid sequence having at least about 95% sequence identity to the amino acid sequence comprising at least amino acid residues 35-244 of SEQ ID NO:66.

305. (New) The isolated or recombinant nucleic acid of claim 304, wherein the wherein the encoded polypeptide comprises an extracellular domain comprising at least amino acid residues 35-244 or 35-245 of SEQ ID NO:66.

306. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises a signal peptide.

307. (New) The isolated or recombinant nucleic acid of claim 306, wherein the signal peptide comprises the signal peptide of human B7-1.

308. (New) The isolated or recombinant nucleic acid of claim 307, wherein the signal peptide comprises an amino acid sequence comprising amino acid residues 1-34 of SEQ ID NO:66.

309. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises a transmembrane domain.

310. (New) The isolated or recombinant nucleic acid of claim 309, wherein the transmembrane domain comprises an amino acid sequence having at least about 90% sequence identity to the amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

311. (New) The isolated or recombinant nucleic acid of claim 309, wherein the transmembrane domain comprises an amino acid sequence having at least about 95% sequence identity to the amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

312. (New) The isolated or recombinant nucleic acid of claim 311, wherein the transmembrane domain comprises an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

313. (New) The isolated or recombinant polypeptide of claim 309, wherein the polypeptide comprises an amino acid sequence having at least about 90% sequence identity to the amino acid sequence corresponding to the extracellular domain and transmembrane domain of SEQ ID NO:66 which comprises at least amino acid residues 35-268 or 35-272 of SEQ ID NO:66.

314. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide further comprises a cytoplasmic domain.

315. (New) The isolated or recombinant nucleic acid of claim 314, wherein the cytoplasmic domain comprises an amino acid sequence having at least about 90% sequence identity to the amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

316. (New) The isolated or recombinant nucleic acid of claim 315, wherein the cytoplasmic domain comprises an amino acid sequence at least comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

317. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises an amino acid sequence having at least about 95% sequence identity to the amino acid sequence comprising at least amino acid residues 35-303 of SEQ ID NO:66.

318. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises an amino acid sequence having at least about 95% sequence identity to the amino acid sequence comprising at least amino acid residues 35-268 or 35-272 of SEQ ID NO:66.

319. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide comprises an amino acid sequence having at least about 95% sequence identity to the amino acid sequence comprising at least amino acid residues 1-268 or 1-272 of SEQ ID NO:66.

320. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide has at least about 95% sequence identity to the full length amino acid sequence of SEQ ID NO:66.

321. (New) The isolated or recombinant nucleic acid of claim 302, wherein the polynucleotide sequence is selected from the group consisting of:

(a) a polynucleotide sequence encoding the full length amino acid sequence set forth in SEQ ID NO:66;

(b) the polynucleotide sequence set forth in SEQ ID NO:19;

(c) a polynucleotide sequence that, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions to the complement of the polynucleotide sequence of (a) or (b); and

(d) a polynucleotide sequence complementary to the polynucleotide sequence of (a) or (b).

322. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide has a human CD28/human CTLA-4 binding affinity ratio greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 and/or induces a T-cell proliferation or activation response about equal to or greater than that induced by human B7-1.

323. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide has a binding affinity for human CD28 that is at least about equal to or greater than the binding affinity of human B7-1 for human CD28.

324. (New) The isolated or recombinant nucleic acid of claim 302, wherein the encoded polypeptide has a binding affinity for human CTLA-4 that is less than the binding affinity of human B7-1 for human CTLA-4.

325. (New) An isolated or recombinant nucleic acid comprising a polynucleotide sequence that has at least about 90% sequence identity to a nucleotide sequence encoding an extracellular domain, said nucleotide sequence comprising at least nucleic acid residues 103-732 of SEQ ID NO:19, wherein said nucleic acid encodes a polypeptide that has a human CD28/human CTLA-4 binding affinity ratio about equal to or greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 and/or induces a T-cell proliferation or activation response when expressed on a cell or bound to a cell membrane, or a complementary polynucleotide sequence thereof.

326. (New) The isolated or recombinant nucleic acid of claim 325, wherein the polynucleotide sequence comprises at least nucleic acid residues 103-732 or 103-735 of SEQ ID NO:19, or a complementary polynucleotide sequence thereof.

327. (New) The isolated or recombinant nucleic acid of claim 325, further comprising a nucleotide sequence encoding a signal peptide.

328. (New) The isolated or recombinant nucleic acid of claim 327, wherein the signal peptide is encoded by a nucleotide sequence selected from the group of:

(a) a nucleotide sequence comprising nucleic acid residues 1-102 of SEQ ID NO:19, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence that encodes amino acid residues 1-34 of SEQ ID NO:66, or a complementary nucleotide sequence thereof; and

(c) a nucleotide sequence which, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions to substantially the entire length of a polynucleotide sequence (a) or (b).

329. (New) The isolated or recombinant nucleic acid of claim 325, further comprising a nucleotide sequence encoding a transmembrane domain.

330. (New) The isolated or recombinant nucleic acid of claim 329, further comprising a nucleotide sequence encoding the transmembrane domain of SEQ ID NO:66.

331. (New) The isolated or recombinant nucleic acid of claim 330, wherein the transmembrane domain is encoded by a nucleotide sequence selected from the group of:

(a) a nucleotide sequence comprising at least nucleic acid residues 733-804 or 736-816 of SEQ ID NO:19, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence that encodes at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66, or a complementary nucleotide sequence thereof; and

(c) a nucleotide sequence which, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions to substantially the entire length of a polynucleotide sequence of (a) or (b).

332. (New) The isolated or recombinant nucleic acid of claim 325, further comprising a nucleotide sequence encoding a cytoplasmic domain.

333. (New) The isolated or recombinant nucleic acid of claim 332, comprising a nucleotide sequence encoding a cytoplasmic domain of SEQ ID NO:66.

334. (New) The isolated or recombinant nucleic acid of claim 333, wherein the cytoplasmic domain is encoded by a nucleotide sequence selected from the group of:

(a) a nucleotide sequence comprising at least nucleic acid residues 734-909 or 817-909 of SEQ ID NO:19, or a complementary nucleotide sequence thereof;

(b) a nucleotide sequence that encodes amino acid residues 269-303 or 273-303 of SEQ ID NO:66, or a complementary nucleotide sequence thereof; and

(c) a nucleotide sequence which, but for the degeneracy of the genetic code, hybridizes under at least stringent conditions to substantially the entire length of a polynucleotide sequence of (a) or (b).

335. (New) The isolated or recombinant nucleic acid of claim 325, wherein the encoded polypeptide has a human CD28/human CTLA-4 binding affinity ratio greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1.

336. (New) The isolated or recombinant nucleic acid of claim 325, wherein the encoded polypeptide induces a T-cell proliferation or activation response about equal to or greater than that induced by human B7-1.

337. (New) The isolated or recombinant nucleic acid of claim 325, wherein the polynucleotide sequence has at least about 90% sequence identity to a nucleotide sequence comprising at least nucleic acid residues 1-732 of SEQ ID NO:19, or a complementary polynucleotide sequence thereof.

338. (New) The isolated or recombinant nucleic acid of claim 325, wherein the encoded polypeptide comprises a signal peptide, extracellular domain, and transmembrane domain, and the polynucleotide sequence has at least about 90% sequence identity to a nucleotide sequence comprising at least nucleic acid residues 1-804 or 1-816 of SEQ ID NO:19, or a complementary polynucleotide sequence thereof.

339. (New) The isolated or recombinant nucleic acid of claim 325, wherein the encoded polypeptide comprises an extracellular domain, transmembrane domain, and cytoplasmic domain, and the polynucleotide sequence has at least about 90% sequence identity to a nucleotide sequence comprising at least nucleic acid residues 103-912 of SEQ ID NO:19, or a complementary polynucleotide sequence thereof.

340. (New) The isolated or recombinant nucleic acid of claim 325, wherein the polynucleotide sequence has at least about 90% sequence identity to the nucleotide sequence set forth in SEQ ID NO:19, or a complementary polynucleotide sequence thereof.

341. (New) A composition comprising a nucleic acid of claim 302 and an excipient.

342. (New) The composition of claim 341, wherein the excipient is a pharmaceutically acceptable excipient.

343. (New) A composition comprising a nucleic acid of claim 325 and an excipient.

344. (New) The composition of claim 343, wherein the excipient is a pharmaceutically acceptable excipient.

345. (New) A cell comprising a nucleic acid of claim 302.

346. (New) A cell comprising a nucleic acid of claim 325.

347. (New) A cell comprising a polypeptide of claim 259.

348. (New) A vector comprising a nucleic acid of claim 302.

349. (New) The vector of claim 348, wherein the vector comprises a plasmid, a cosmid, a phage, a virus, a virus particle, or a fragment of a virus.

350. (New) The vector of claim 348, wherein the vector is an expression vector.

351. (New) The vector of claim 350, wherein the nucleic acid is operably linked to a promoter.

352. (New) The vector of claim 350, wherein the vector further comprises a polynucleotide sequence encoding an antigen.

353. (New) The vector of claim 352, wherein the nucleic acid is operably linked to first promoter and the polynucleotide sequence encoding the antigen is operably linked to a second promoter, wherein the second promoter is the same or different from the first promoter.

354. (New) The vector of claim 352, wherein the antigen is a cancer antigen.

355. (New) The vector of claim 354, wherein the cancer antigen is EpCam/KSA.

356. (New) The vector of claim 355, wherein the expression vector comprises the vector shown in Figure 22B.

357. (New) A host cell transformed by a vector of claim 348.

358. (New) A vector comprising a nucleic acid of claim 325.

359. (New) The vector of claim 358, wherein the vector comprises a viral vector.

360. (New) The vector of claim 358, wherein the vector is an expression vector.

361. (New) The vector of claim 360, wherein the nucleic acid is operably linked to a promoter.

362. (New) The vector of claim 360, wherein the vector further comprises a polynucleotide sequence encoding an antigen.

363. (New) The vector of claim 362, wherein the nucleic acid is operably linked to first promoter and the polynucleotide sequence encoding the antigen is operably linked to a second promoter, wherein the second promoter is the same or different from the first promoter.

364. (New) The vector of claim 362, wherein the antigen is a cancer antigen.

365. (New) The vector of claim 364, wherein the cancer antigen is EpCam/KSA.

366. (New) The vector of claim 365, wherein the expression vector comprises the vector shown in Figure 22B.

367. (New) A host cell transformed by a vector of claim 358.

368. (New) A polypeptide which is specifically bound by a polyclonal antisera raised against the polypeptide of claim 259.

369. (New) An antibody or antisera which specifically binds a polypeptide of claim 259.

370. (New) A method of producing a polypeptide, the method comprising:

(a) introducing into a population of cells a nucleic acid of claim 302, the nucleic acid operatively linked to a regulatory sequence effective to produce the encoded polypeptide;

(b) culturing the cells in a culture medium to produce the polypeptide; and

(c) isolating the polypeptide from the cells or from the culture medium.

371. (New) A method of producing a polypeptide, the method comprising:

(a) introducing into a population of cells the expression vector of claim 350;

(b) administering the expression vector into a mammal; and

(c) isolating the polypeptide from the mammal or from a byproduct of the mammal.

372. (New) A method of producing a polypeptide, the method comprising:

(a) introducing into a population of cells the expression vector of claim 358;

(b) administering the expression vector into a mammal; and

(c) isolating the polypeptide from the mammal or from a byproduct of the mammal.

373. (New) A method for modulating an immune response in a mammal, the method comprising administering to cells of the mammal a nucleic acid of claim 302, wherein the nucleic acid is operably linked to a promoter, in an amount sufficient that sufficient expression of the encoded polypeptide results, to modulate an immune response in the mammal.

374. (New) The method of claim 373, further comprising administering to cells of the mammal a polynucleotide encoding an antigen specific for a disease or disorder, wherein the polynucleotide is operably linked to a promoter, in an amount sufficient that sufficient expression of the encoded polypeptide results, such that the nucleic acid modulates the immune response induced by the antigen.

375. (New) The method of claim 374, wherein the nucleic acid enhances the immune response induced by the antigen.

376. (New) The method of claim 373, wherein the nucleic acid is administered in vivo to the mammal.

377. (New) The method of claim 373, wherein the nucleic acid is administered in vitro or ex vivo to cells of the mammal.

378. (New) The method of claim 374, wherein the antigen is a cancer antigen.

379. (New) A method for inducing a T-cell proliferation response in a mammal, the method comprising administering to the mammal a nucleic acid of claim 302, wherein the nucleic acid is operably linked to a promoter, in an amount sufficient that sufficient expression of the encoded polypeptide results, to induce the T-cell proliferation response in the mammal.

380. (New) A method for inducing an effective immune response to an antigen in a mammal, the method comprising administering to a mammal, which mammal is exposed to the antigen, a polynucleotide comprising a nucleic acid of claim 302, wherein the nucleic acid is operably linked to a promoter, in an amount sufficient that sufficient expression of the encoded polypeptide results, to induce an effective immune response to the antigen.

381. (New) The isolated or recombinant nucleic acid of claim 325, wherein the polynucleotide sequence comprises at least nucleic acid residues 1-735 of SEQ ID NO:19.--